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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,169	07/25/2001	Alan John Kingsman	674523-2005.1	8430

7590 10/25/2002

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EXAMINER
NGUYEN, DAVE TRONG

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/915,169	Kingsman
Examiner	**Art Unit**
Dave Nguyen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 25, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *20-90* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *20-90* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *09/224,014* .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claim 1-19 have been canceled, claims 20-90 have been added by the preliminary amendment filed July 25, 2001.

Claims 20-90, to which the following grounds of rejection are applicable, are pending.

The examiner acknowledges that certified copies of the two British Applications, 9621680 and 9624457, filed 10/17/96 and 11/25/96, respectively, are present in application 09/224,014, now US Pat No. 6,312,682.

The cross-reference to the allowed US 09/224,014 needs to be updated since the '014 application is now issued as US Pat No. 6,312,682.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20-90, readable on a genus of functional equivalents of a rev protein, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompasses a genus of nucleotide sequences encoding a functional equivalent of a a lentiviral rev protein.

The specification coupled with the state of the prior art provides sufficient description of a DNA encoding a lentiviral rev protein or a constitutive transport element (CTE found in Mason Pfizer monkey virus). The specification does not define nor provide any disclosure of a representative number of species of "functional equivalents" as intended by applicant's breadth of the claims.

An adequate written description of the invention defined by the claims, *e.g.* genus of lentiviral vectors and genus of DNA sequences comprising a "functional equivalent" encoding nucleic acid, requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of lentiviruses and corresponding DNA sequences which are claimed to encode a product that is functionally equivalent to a lentiviral rev. It is not sufficient to have one single species of the CTE and to define DNA solely by its principal biological property, i.e., functional equivalents, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any or all other functional equivalent coding sequences as encompassed by the claimed invention, and yet to be discovered or identified. In addition, a nucleic acid sequence encoding a particular protein determines the protein' s structural, and functional properties, and an envision of a representative number of "functional equivalent" sequences that may retain similar functions to the disclosed HIV RREV sequence, for example, requires a knowledge of and guidance with regard to which amino acids in the protein' s sequence and/or nucleotides in the DNA, if any, are tolerant of modification and which are conserved (*i.e.,* expectedly intolerant to modification), and detailed knowledge of the ways in which a protein' s structure relates to its functional usefulness (Ngo *et al.,* in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz *et al.,* (ed.), Birkhauser, Boston, MA, pp. 492-495). Claiming all DNA's and/or vectors or methods of employing specific combinations of vectors that achieve a result without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed genus.

Claim 20-90 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

The subject maters as being sought in the presently pending claims, with a provision that any limitation reciting "functional equivalents thereof" is not encompassed and recited by the enabled claimed subject matters.

The specification does not reasonably provide enablement for DNA sequences corresponding to any and/or functional equivalents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

When given their broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including unspecified "functional equivalent" lentiviral sequences encoding for an unspecified lentiviral amino acid sequences which must exhibit an biological function equivalent to a lentivral rev. However, the specification fails to provide an enabling disclosure for what such polynucleotides would comprise other than lentiviral rev sequences and the CTE (CTE found in Mason Pfizer monkey virus), particularly applicant was not in possession of the claimed genus. In addition, it is not apparent how one skilled in the art determines which of the unspecified "equivalent" encoding polynucleotide sequences as claimed encodes a useful product such a gene(s) encoding a protein(s) involving packaging and production of replication defective lentiviral virions, without undue experimentation, particularly on the basis of applicant's disclosure. The use of the claimed DNA sequences as functional equivalent without an adequate description thereof represents an invitation to experiment, wherein the skilled artisan is invited to elaborate a functional use for DNA sequences. Furthermore, the invention as defined by the claims is drawn to undisclosed nucleic acids that are not required to have any particular

degree of sequence identity and may not necessarily encode any putative proteins that the nucleic acids encompassed by the claimed invention might encode. Thus, given the lack of guidance and direction in regard to what the polynucleotides defined by the claims would comprise and how one would use such, the artisan would be required to exercise undue experimentation in practice of the invention. Note that the Court of Appeals for the Federal Circuit has ruled that claims that embrace a large number of species of polynucleotide sequences without proper guidance in the application as to how to make and use such polynucleotides do not meet the requirements of 35 U.S.C. § 112, first paragraph, *Amgen v Chugai* (18 USPQ2d 1016 (Fed. Cir. 1991)).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-90 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims1-71 of U.S. Patent No. 6312,682. Although the conflicting claims are not identical, they are not patentably distinct from each other because

While the examined claims claim and recite a "functional equivalent" to a lentivral rev, which limitation is not recited in the patent claims, the examined claims also disclose every limitation as recited in the patent claims. Thus, the subject matter being sought in the examined claims do anticipate the subject matter being sought in the patent claims.

During a telephone conversation with attorney Thomas Kowalski on October 16, 2002, applicant and the examiner discuses a proposed claim that may be introduced by applicants subsequent to this office action. The proposed claim is directed to a packaging plasmid vector that expresses only lentiviral gag and lentivral pol proteins, as shown in Fig 1 of the as-filed specification, the examiner indicates to applicant that such proposed claim not only does not reflect the subject matter being sought in the pending claims, *e.g,* claims 20-90, the proposed claim may have potential prior art issues. For example, in Verma *et al.* (US Pat NO. 6,013,516), claims 1 and 4 discloses and claims a four vector system, wherein one of the four vectors is a packaging plasmid vector consists essentially of a non-lentiviral promoter operably linked to a lentiviral gag and pog genes. Applicant indicates that applicant will study this office action and the examiner's comments with regard to applicant's proposed claim prior to considering submitting a response to this office action.

The following issued patents are found relevant to the subject matter being sought in the presently pending claims:

US patent No. 6,326,007, Yilma et al., EFD: 7/20/95, on column 1, middle of the last paragraph, discloses, teaches and suggests that lentiviral or HIV vif, vpr, vpu, vpx, and nef genes can be deleted without completely abrogating the ability of the virus to replicate. However, the '007 patent does not teach or suggest that lentiviral tat can be deleted without abrogating the ability of a lentiviral virus to replicate. In fact, Weiner et al., US Pat No. 5,981,505, column 50, lines 4-7, discloses that "the Tat protein is a transactivator of LTR-directed gene expression", and that "it is absolutely essential for HIV replication". While Naldini *et al.* (US Pat No. 6,428,953) discloses, teach and suggest the subject matter being sought in the presently pending claims on column 8, lines 24-48, the '953 patent is not prior art against this as-filed application, particularly since this as-filed application not only is a CON of PCT/GB97/02857, filed 10/17/9, but also does enjoy a priority claim to British Applications, 9621680 and 9624457, filed 10/17/96 and 11/25/96, respectively.

No claim is allowed.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst Dianiece Jacobs, whose telephone number is **(703) 305-3388.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Trong Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER